THE COMMONWEALTH OF MASSACHUSETTS
EXECUTIVE OFFICE OF ENVIRONMENTAL AFFAIRS
Department of Agricultural Resources
251 Causeway Street, Suite 500, Boston, MA 02114
617-626-1700 fax 617-626-1850 www.Mass.gov/DFA

MITT ROMNEY
Governor

KERRY HEALEY
Lieutenant Governor

ELLEN ROY HERZFELDER
Secretary

DOUGLAS P. GILLESPIE
Commissioner

SULFOMETURON METHYL

COMMON TRADE NAME(S):	Oust
CHEMICAL NAME :	N-[4,6-dimethylpyrimidin-2-yI) amino-carbonyl -2-methoxycarbonylbenzenesulfonaflhide
CAS NO:	74222-97-2

GENERAL INFORMATION

Sulfometuron methyl, the active ingredient in the herbicide Oust, is a member of the group of sulfonylurea herbicides. Sulfometuron Methyl is a broad-spectrum selective weed control agent used in non-crop areas. Oust is applied pre- or post-emergence which provides control against many broad-leaf weeds and grasses through contact and residual activity. (15)

ENVIRONMENTAL FATE

Mobility

The mobility of sulfometuron methyl has been reported in literature and the database available is complete. Sulfometuron methyl is a weak acid (pKa 5.2) and consequently, adsorption coefficients were calculated for various soils at pH values of 5, 6, and 7. In a low organic matter I soil (1%) the adsorption coefficients were 2.0, 0.8 and 0.3 at the respective pH values. This study indicates that sulfometuron methyl is more strongly adsorbed to soil as the pH decreased, and as organic matter increases. (15)

Soil thin layer chromatography and adsorption coefficients were performed and calculated for four standard soils. Kd values ranged from 0.71 to 2.85 and Rf values ranged from 0.33 to 0.85 indicated a moderate mobility. In addition, soil column studies using the same four soils indicate a moderate to moderately high mobility pesticide. Koc values calculated from the soil Kd values range from 61 to 122 which is lower than the EPA guideline of 400. (101)

In a field mobility study, sulfometuron methyl was applied to soil tubes in five locations (Delaware, North Carolina, Oregon, Colorado, and Saskatchewan, Canada) at a rate of 1 lb a.i./Acre. There was no report of rainfall

at these sites. Each application was made at a different time making it difficult to compare results. Samples were taken for a minimum of a year and at some for two years, and at 8 cm (3 in) intervals to 32 cm (12 inches). Results indicate that sulfometuron methyl is moderately mobile under most conditions. One surprising fact is that immediately after application, all locations had detectable residues in a layer below the top layer of soil, and in two locations (Colorado and Oregon) in the deepest layer sampled. All locations except Delaware also had detectable residues at the 24-32 cm layer at other times during the study. There are also indications that sulfometuron methyl would leach further than the deepest soil layer which was sampled. (102)

Persistence

Sulfometuron methyl is degraded by microbial action, photo-decomposition and by hydrolysis at acidic pH's. The photolysis half-life on soil is between 1 to 2 weeks and in distilled water, approximately 160 hours. The hydrolysis half-life at pH 2 and 5 is 100 and 475 hours respectively. At neutral or basic pH's, sulfometuron methyl is stable to hydrolysis. (15,100, 101)

Reports indicate that the overall rate of sulfometuron methyl degradation in soil depends on pH and soil moisture content. Half-lives of one week were reported under laboratory conditions, but field studies at neutral pH revealed greater persistence. Increased soil moisture content resulted in increased degradation rates, but only approximately 10%. (15, 101)

The soil half-life is reported as four weeks with longer times in colder conditions. A review of available studies, however reveals that the shortest half-life was six weeks in Delaware. In the same study the half-life ranged from six weeks to one year in Oregon. (15, 102)

The reported half-life of four weeks is relatively short and would not be cause for concern. However, it seems evident that in most circumstances it may be significantly longer. In all cases reported in this study, the half-life was six weeks or longer and a more realistic estimate may be closer to two months. Another point discussed in the literature is the lack of any significant degradation during the cold periods of the year. Applications in the late fall could lead to longer half-lives and thereby more potential for increased leaching.

The field study discusses the faster degradation rates of sulfometuron methyl in the east as possibly attributable to the more acidic and moister soils in the east. This is certainly true and may in fact have contributed to shorter half-lives, but a point which is not discussed was the timing of the applications. The two western sites were treated in early to mid-July, whereas the western sites were treated in the fall. Saskatchewan was treated in late July, but the climate at that location is cooler and becomes much colder.

TOXICITY REVIEW

Five animals per sex per group were gavaged with sulfometuron methyl suspended in corn oil at a dosage of 5,000 mg/kg. Gross pathological examination revealed slight weight increase in the lungs that were pale red with grey foci in males and similar lung effects in one female. In addition, four females had a pink thymus and one had a slight liver weight. The oral LD50 in male and female ChR-CD rats was determined to be greater than 5,000 mg/kg. (110)

The inhalation LC5O was tested in groups of five male and five female Crl:CD rats. Rats were exposed to control air or test concentrations of either 6.4 or 11 mg/L. There were no clinical or pathological differences between controls or test groups. The inhalation LC5O was greater than 5.0 mg/L (111) while sulfometuron methyl was tested at 6.4 and 11 mg/L. The EPA cutoff for LC5O concentration is 5 mg/L.

Acute skin absorption LD5O tests were performed on five male and five female New Zealand white rabbits. Doses of 2,000 mg/kg of pesticide were applied to abraded skin on the back of the rabbit. Clinical signs in males

were sporadic weight loss, slight erythema 1 to 2 days after treatment and diarrhea at 11 days. Gross pathological examination showed no changes due to the test material. The dermal LD5O in rabbits was greater than 2,000 mg/kg. (112)

In a separate acute dermal LD5O test, four groups of five adult male and one group of five adult female New Zealand rabbits were used. Groups of males were dosed at the following levels: 1,500 mg/kg, 2,000 mg/kg, and 8,000 mg/kg and the females were dosed at 2,000 mg/kg. Clinical signs in all the groups of males were moderate to mild redness and sporadic weight loss. The animals in the two highest dose experienced mild swelling, the 2,000 mg/kg group showed moderate swelling while the 1,500 mg/kg group had slight swelling. Clinical signs in the females were severe to mild redness, severe to slight swelling and sporadic weight loss. There were no compound related pathological observations. There was one death in the male 2,000 kg/mg group, but it was not believed to be related to the compound. The LD5O for the acute skin absorption in rabbits was greater than 2,000 mg/kg. (116)

Eye irritation studies were performed by placing 10 mg of solid test material in the conjunctival ac of each of two albino rabbits. There were no corneal or iritic effect. However, there was redness (1 hour to 1 day; not washed eyes and mild for 1 hour unwashed eyes); swelling (1 to 4 hours unwashed eyes) and no discharge was observed. Both washed and unwashed eyes were normal within 1 to 2 days. (113)

In guinea pigs, both primary skin irritation and sensitization tests were run. Ten animals per group were exposed to 0.05 ml of either a 50% or a 5% suspension of sulfometuron methyl. The 50% suspension showed mild to no skin irritation response in 24 hours and no irritation at 48 hours. The 5% suspension reproduced no skin irritation. There was no sensitization response. (114)

The oral LD5O test was conducted with the formulation using young male and female adult Crl:CD rats, five rats per group. 5,000 mg/kg was administered by gavage in a 25% suspension in corn oil. The only clinical finding was alopecia in males. Gross pathological examination showed in both males and females slightly heavy lungs that were pale to pale red with red to dark red foci and white mottling in 1 to 3 animals. The LD5O is greater than 5,000 mg/kg. Additionally in a range finding study, no mortalities were seen in doses from up to 7,500 mg/kg. (115)

Nine male albino rabbits were tested for eye irritation studies. The right eyes were treated with 0.1 ml (61.8 mg) of test material. The left eyes served as untreated controls. Results indicated a transient localized area of slight corneal cloudiness in 2 of the 6 unwashed eyes. The eyes returned to normal in 2 to 3 days. Two of the three eyes treated and washed showed a transient localized area slight corneal cloudiness and mild conjunctivitis with no iritic effects. The washed eyes returned to normal within 3 to 4 days. This compound was considered a slight to mild irritant. (117)

Skin irritation tests were conducted on six male albino rabbits. Doses of 0.5 g of solid pesticide (moistened with saline) were applied to two intact and two abraded skin areas on each rabbit. Each rabbit serves as its own control; treated areas were compared to adjacent untreated areas. Observations and scoring were done by the method of Draize (118) and at 24 and 72 hours after exposure. The compound was not found to be a primary irritant on either intact or abraded skin of rabbits. (119)

Primary skin irritation tests were performed on ten guinea pigs. The procedure was the same as used in testing the technical sulfometuron methyl. Doses of 0.05 ml of a 50% suspension of the pesticide in dimethyl phthalate were used. The 50% suspension caused mild to no irritation in five of the animals. No irritation was caused by the 5% suspension. No sensitization response was observed. (120)

Subchronic and Chronic Studies (Mammalian)

Male and female CD-i mice were fed diets to which had been added 0, 100, 1,000, or 7,500 ppm (0, 13.3, 133, or 997 mg/kg) (a) sulfometuron methyl for 90 days. Hematological evaluations were conducted on all mice (tail cut bleeding at approximately 1, 2 and 3 months after study initiation. All mice were sacrificed and necropsied at 90 days. Organs were weighed and examined histologically. Male mice fed the diet containing 7,500 ppm pesticide showed reduced mean body weights and weight gains. Growth of the 100 and 1,000 ppm groups of males and all treated females was the same as that in the control group. No mortalities occurred. (121)

Hemolytic effects were seen as a result of dietary exposure to sulfometuron methyl in all groups. Significant increases in leukocyte count were found in the 7,500 ppm (997 mg/kg) males. There were statistically significant changes in other blood parameters that were not dose related. Mean absolute and relative liver weights were elevated in all male treatment groups. Histological examination revealed bile stasis in five of ten males in the 7,500 ppm group. In the females, a slight increase in relative liver weight and increased hepatocellular cytoplasmic granularity was observed. Decreases in both mean and relative thymus weights were observed in all treated male groups. Thymic cortical atrophy occurred in three males in the 7,500 ppm group and one male in the 100 ppm group. Because of low frequency of occurrence 7,500 and 100 ppm and absence in the 1,000 ppm group, the thymic cortical atrophy is not considered to be related to the decreased thymus wrights. Based on the observed hemolytic effect, there was no NOEL from this study.

In a second mouse study, five groups of 80 males and 80 female Crl:CD-1 (1 CR)BR mice were fed diets containing one of the following concentrations of sulfometuron methyl: 0. 5, 20, 100, or 1,000 ppm (0, 0.66, 2.66, 13.3,133 mg/kg) for 18 months. Food consumption was monitored throughout the study, mice were weighted and hematological evaluations were performed at regular intervals. At 18 months, mice were sacrificed and necropsied. Mean body weights and mean body weight gains in all treatment groups except for the 1,000 ppm female group were comparable to control groups. Sporadic changes in weight gain were observed in that group.

(a) In these discussions the assumptions made for conversion of ppm (diet) to mg/kg/D were:

SPECIES	**BODYWEIGHT (kg)**	**INTAKE ((kg)**
Rat	0.35	0.020
Mouse	0.03	0.004
Dog	10	0.4

(133)

When data was presented as ppm the does was estimated in mg/kg and is presented in parenthesis.

Mild anemia was observed in the female 1,000 ppm group as evidenced by statistically significant decreases in erythrocyte count, hemoglobin concentration and hematocrit. There was also a significant increase in mean corpuscular volume and platelet count. While the hematological results appear to differ from those in the 90 day mouse study, the data indicate that there were several statistically significant changes in some blood parameters at the three month (90 day) sampling time which were not apparent at other sampling times. However, although reticulocyte smears were made, they were not evaluated and it cannot be ascertained that a response to a hemolytic effect actually occurred. If it did, a NOEL in this strain of mice for a hemolytic effect at 90 days in the 18 month study would be 5 ppm. There was a non-dose related but, statistically significant increase in the incidence of amyloidosis in the female 1,000 ppm groups, but no specific target organ was identified. The overall NOEL for dietary intake of sulfometuron methyl for male and female mice was 1,000 ppm (133 mg/kg) and 100 ppm (13.3 mg/kg) respectively under the conditions of this study based on body weight, body weight gain, clinical pathology and pathological findings. (124)

Groups of 16 male and 16 female CD rats were fed diets containing 0, 100, 1,000, 5,000 ppm (0, 5.7 57, 285 mg/kg) sulfometuron methyl. At 1, 2 and 3 months after the study initiation, hematological, urological and clinical chemistry evaluations were performed. At the end of the study, ten rats from each group were sacrificed and evaluated pathologically. There were no differences between treatments and controls in body weight, weight gain, food consumption and food efficiency. There were no mortalities. The only clinical sign observed was alopecia in three males in the 100 ppm group. The male 5,000 ppm treatment group showed slightly elevated mean leukocyte counts, increased mean relative number of lymphocytes and decreased mean relative number of neutrophils. Due to the effects of white blood cells in male 5,000 ppm group, the NOEL dietary concentration i this study was 1,000 ppm (56 mg/kg/D). (122)

Four groups of five male and five female New Zealand white rabbits were dermally exposed to either 1, 125, 500, or 2,000 mg/kg, six hours per day for 21 consecutive days. After the exposure period, three male and three female rabbits per group were sacrificed for pathological evaluation. The remaining two males and two females from each group were sacrificed and evaluated pathologically following a two week recovery period. Clinical signs observed in rabbits from all test groups including controls were sporadic weight loss and diarrhea. Histopathological and clinical pathological examination showed no compound-related effects. One rabbit did after the eighth dose from causes not related to the test substance. (123)

Groups of 80 male and 80 female Crl:CD (SD) BR rates were fed diets containing 0, 50, 500 or 5,000 ppm (0, .8, 28.5, or 285 mg/kg) sulfometuron methyl for approximately two years. Hematological, clinical chemistry and urological testing was conducted a 3, 6, 9,12,18, and 24 months. After 12 months, ten male and ten female rats per group were randomly selected, sacrificed and pathologically examined. At 24 months, all surviving rats were sacrificed, necropsied, and examined pathologically.

In the female 5,000 ppm group, food consumption throughout the study was slightly depressed and overall mean weight gain during the first year and mean body weights during the second year were significantly depressed. There were no abnormalities in appearance or behavior observed during the study.

Decreased erythrocyte count and hematocrit in the male 500 and 5,000 ppm groups were observed at the 24 month clinical evaluation suggesting a minimal dose-related hemolytic effect. There were no other compound related hematological, clinical chemistry or urological abnormalities observed. Mean absolute brain weights were significantly lower in the male 5,000 ppm group at both one and two sacrifice times. However, no abnormal gross or histological observation were noted. Mean relative and absolute thymus weight of the 500 and 5,000 ppm males was decreased compared to controls at terminal sacrifice. Mean testes weights of rats in the 5600 and 5,000 ppm groups were less than controls.

Histological examinations revealed dose-dependent increases in the incidence of bile duct hyperplasia and fibrosis in the female 500 and 5,000 ppm groups at the two year sacrifice. Severity of the lesions were minimal to mild, suggesting a slightly toxic effect of sulfometuron methyl on the livers of these female rats.

The NOEL in this strain of rat under these study conditions was 50 ppm (2.8 mg/kg/D). (125)

Oncogenicity Studies

Oncogenic endpoints were evaluated in the chronic mouse and rat studies for sulfometuron methyl. Cr1: CD-i (1 CR) BR mice received 0, 5, 20, 100, or 1,000 ppm sulfometuron in the diet of 18 months. There were no compound related increases in tumor incidence (124). CRL:CD (SD) BR rats received 0, 50, 500, or 5,000 ppm sulfometuron in the diet for two years. There was no increase in frequency of occurrence of tumors in these rats (125). Sulfometuron methyl is not carcinogenic in rats and mice under these conditions.

Mutagenicity Testing

The Ames Salmonella/microsome assay tested the ability of Sulfometuron methyl to revert four strains of Salmonella typhimurium from histidine dependence to histidine independence. The assay was performed both with and without a rat liver homogenate (S-9) activation system. The test substance was found not to be mutagenic for these strains of bacteria under the test conditions at doses from 2.5 to 1,000 mg/plate. (129)

Frequency of chromosome aberrations was tested in CHO cells both with and without metabolic activation (S-9). The doses tested ranged from 300 ug/mI to 10 ng/ml in a half log series. No increase in chromosome aberrations was observed in culture exposed under the test conditions to these concentrations of the test material. (130)

The CHO cell line was used to test mutations in the gene coding for the enzyme hypoxanthineguanine phosphoribosyl transferase (HGPRT) both in the presence and absence of an activation (S-9) system. Concentration of the test material ranged from 0 to .1 mM. No mutagenic activity was detected. (131)

The ability of sulfometuron methyl to induce unscheduled DNA (UDS) synthesis in freshly isolated rat hepatocytes was tested. Concentrations of test material ranged for 1 X 10 -5 to 1.0 mM in half log increments. Under these test conditions, no induction of UDS was detected. (132)

Developmental Studies

Groups of 17 female artificially inseminated rabbits wee gavaged with test material on days 6 to 18 of gestation. Dosage levels were 0, 30, 100, and 300 mg/kg suspended in 0.5% methylcellulose in water. Animals were sacrificed on day 29 of gestation and fetuses wee removed by cesarean section. No treatment-related effects were observed in the maternal clinical observations or gross pathology. There were no statistically significant differences between control and treatment groups in any of the other parameters measured (maternal body weight changes, clinical observations, survival, gross pathology pregnancy rates, numbers and percentages of corpora lutea, implantations, resorptions in each maternal animal, fetal sex, viability and development). Under the conditions of this study, sulfometuron methyl was not considered to be teratogenic in New Zealand white rabbits. (127)

A teratology study was conducted using female Crl:CD (SR) BR rats which were fed a diet containing sulfometuron methyl. Concentrations of 0, 50, 1,000, and 5,000 ppm were used. Thirty-five rats were used as controls, 25 rats were assigned to the 50 and 1,000 ppm group and 15 rats were assigned to the 5,000 ppm group. Rats were fed the test diet on days 6 to 15 of gestation and sacrificed on day 21 of gestation for gross and histological examination. (128)

Rats on the highest dose level gained significantly less weight and ate significantly less feed than controls. The fetuses of this exposure group weighted significantly less than those of the control dams. No other adverse effects were noted in the lower exposure groups. No teratogenicity was demonstrated in this study. The minimum effect level of maternal toxicity and embryofetal toxicity was 5,000 ppm (286 mg/kg) and the NOEL under these study conditions was 1,000 ppm (57 mg/kg). (128) Reproductive studies were performed in conjunction with the 90 day feeding study in rats and the two year feeding study in rats.

In the 90 day feeding study (122), six male and six female rats which had been fed diets obtaining 0,100,1,000, and 5,000 ppm of sulfometuron methyl (for 90 days) were mated and delivered litters. No adverse effects were observed as indicated by fertility, gestation, viability and lactation indies. In addition, there wee no differences between treatment and controls in the mean body weights and survival of weaning pups.

In the two year feeding study (125), 20 rats per group were used in a two generation, four litter reproduction study, initiated 90 days after the start of the long-term feeding study. Fo rats were mated. Females were allowed to

give birth and Fla pups wee followed until weaning (21 days) at which time they were sacrificed. Fo females wee again mated, but to different Fo males. Fib pups were delivered and observed. At weaning, 20 males and 20 females were selected from each dietary level (0, 50, 500, and 5,000 ppm) and continued on the treatment for 90 days. Fib rats were bred twice within their respective group, producing F2a and F2b litters. Ten males and ten females from the F2b litters were sacrificed and examined histologically. (125)

During the 90 day feeding period for Fl b rats, body weight and diet consumption were decreased in the female 5,000 ppm group. The number of pus born and the number of pups born alive to the 5,000 ppm groups was consistently lower in both the Fl and F2 generations and was statistically significant for F2b litters. Decreased pup counts may reflect the general health status of the mother as evidenced by decreased body weight and diet consumption of the Fl b 5,000 ppm group. No gross or histopathological changes or effects on organ weights were observed in the weaned F2b rats. The NOEL established, based on this sub-study was 500 ppm (28 mg/kg). (125)

Avian Toxicity

Sulfometuron methyl has been tested in the bobwhite quail and the mallard duck. The **8** day dietary LC5O's were greater than 5,620 and 5,000 ppm respectively. The acute oral LD5O in the mallard duck was greater than 5,000 mg/kg. (101)

Invertebrate Toxicity

The aquatic invertebrate, Daphnia magna was tested and the 48 hour LOSO was greater than 12.5 ppm sulfometuron methyl. (15)

Aquatic Toxicity

Species tested on the aquatic toxicity studies include bluegill sunfish (96 hour) and rainbow trout (96 hour). In both cases the LC5O was greater than 12.5 ppm.

A life stage study was done using the fathead minnow. There were no effects observed on embryo hatch, larval survival or growth at concentrations of 1.2 mg/L or less. (15)

SUMMARY

Sulfometuron methyl is a material both moderately mobile and moderately persistent. A closer look at the material however, reveals that the Oust is applied at the average rate of five ounces of product (3.75 oz a.i.)/acre or 106 grams per acre. These studies were conducted with applications of 1 lb a.i./acre. The lower application rates both minimize the persistence of sulfometuron methyl in soil and thereby diminish the amount of material which is available to leach through the soil. Therefore, sulfometuron may be used if the application rates are kept sufficiently low. This is because the soil organic material and soil microorganisms are able to absorb and degrade lower rates of pesticides.

The oral LD50 in rats for sulfometuron methyl is greater than 5,000 mg/kg and the dermal LD5O is greater than 2,000 mg/kg in rabbits.

The sub-chronic and chronic NOELS are 50 ppm (2.8 mg/kg/D) in rates; 200 ppm (i mg/kg/D) in dogs; and 5 ppm (0.66 mg/kg/D) at 90 days for the reversible hemolytic effect and 100 ppm (13.3 mg/kg/D) at two years in the mouse. This makes the mouse at 90 days the most sensitive species with a transient hemolytic effect, to sulfometuron methyl exposure.

REFERENCES

15. Pesticide Background Statements August 1984 USDA Forest Service A g r i c u It u r a I Handbook # 633, Vol. 1.

100. DuPont Technical Data Sheet for Sulfometuron methyl.

101. Properties of Sulfometuron Methyl Affecting Its Environmental Fate: Aqueous Hydrolysis and Photolysis, Mobility and Adsorption on Soils and Bioaccumulation Potential. 1985: J. Agr. Food Chemistry; 33: 590.

102 Environmental Fate of Sulfometuron Methyl in Aerobic Soils. J. Agr. Food Chemistry, 1985, 33: 596.

110. 1980. Oral LD5O Test in Rats: Haskell Laboratory Report No. 870-80 E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

111. 1982. Inhalation Median Lethal Concentration (LD5O) of INT-5648-18 by EPA Protocol: Haskell Laboratory Report No. 657-82. E.I. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

112. 1981. Acute Skin Absorption LD5O Test on Rabbits: Haskell Laboratory Report No. 1978-80. E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

113. 1979. Eye Irritation Test in Rabbits: Haskell Laboratory Report No. 230-79. EL du Pont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine Newark, DE.

114. 1979. Primary Skin Irritation Test and Sensitization Tests on Guinea Pigs: Haskell Laboratory Report No. 232-79. E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

115. 1980. Oral LD5O in Rats: Haskell Laboratory Report No. 965-80. E.I. duPont d e Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

116. 1980. Acute Skin Absorption LD50 Test on Rabbits: Haskell Laboratory Report No. 1068-60 E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

117. 1980. Eye Irritation in Rabbits: Haskell Laboratory Report No. 963-80. E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

118. Draize, J.H. and Kelley, E.A. 1959. The Urinary Excretion of Boric Acid Preparations Following Oral Administration and Topical Applications to Intact and Damaged Skin of Rabbits. Toxicology & Applied Pharmacology. 1(3): 267-276.

119. 1980. Skin Irritation Test on Rabbits for EPA Pesticide Registration. (HLR 964-80) E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

120. 1980. Primary Skin Irritation and Sensitization Test on Guinea Pigs: (HLR 966-80) Haskell Laboratory Report No. 966-80. E.I. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

121.1981. Ninety-Day Feeding Study with Benzoic Acid, 2-[[(4, 6-Dimethyl-2-pyrimidinyl)-aminocarbonyl], Methyl Ester, INT-5648, in Mice: Haskell Laboratory Report No. 500-81. El. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Indusbial Medicine, Newark, DE.

122. 1980. Ninety-Day Feeding and One Generation Reproduction Study with Benzoic Acid, 2-[[4, 6-Dimethyl-2-pyrimidinyl)-aminocarbonyl] aminosulfonyl], Methyl Ester, INT-5648, in Rats: Haskell Laboratory Report No. 928-80. E.I. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

123. 1982. Subacute Dermal Toxicity Study (21 days) in Rabbits:Haskell Laboratory Report No. 792-82. E.I. duPont de Nemours and Company, Inc. Haskell Laboratory of Toxicology and Industrial Medicine, Newark, DE.

124. Tobia, A.J. 1987. Oncogenicity Study with INT-5648 Long-Term Feeding Study in Mice: Haskell Laboratory Report No. 355-87. **E.I.** duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

125. 1984. Long-Term Feeding Study in Rats with Benzoic Acid, 2-[[[[(4, 6-dimethyl-2-pyrimidinyl) amino]carbonyl]sulfonyl]-,methyl ester (INT-5648): Haskell Laboratory Report No 367-84. E.I., duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.

126. O'Neal, F.O. 1983. One-Year Feeding Study in Dogs with Benzoic Acid, 2- [[[[(4, 6-dimethyl-2-pyrimidinyl) amino] carbonyl] -amino]sulfonyl] -,methyl ester (INT-5648 Haskell Laboratory Report No. 482-82. E.I. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.
127. 1981. Teratology Study in Rabbits, HLO-331-81. Hazleton Laboratories America, Inc. 9200 Leesburg Turnpike, Vienna, VA 22180. Submitted to: E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.
128. 1981. Benzoic Acid 2- [[[[(4, 6-dimethyl-2-pyrimidinyl) amino] carbonyl] amino] sulfonyl] - methyl ester (INT-5648):Teratogencity Study by Diet in the Rat: Haskell Laboratory Report NJ 316-81. E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.
129. 1979. Mutagenic Activity in the Salmonella/Microsome Assay: Haskell Laboratory Report No. 271-79. E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.
130. 1982. Mutagenicity Evaluation of H#13,647-03 in an In Vitro Cytogenic Assay Measuring Chromosome Aberration Frequencies in Chinese Hamster Ovary (CHO) Cells, HLO-792-81. Litton Bionetics, Inc., 5516 Nkiolson Lane, Kensington, MD 290895. Submitted to: E.I. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industria Medicine, Newark, DE.
131. 1981. Chinese Hamster Ovary Cell Assay for Mutagenicity: Haskell Laboratory Report No. 1074-80. El. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.
132. 1982. Unscheduled DNA Synthesis/Rat Hepatocytes in Vitro:Haskell Laboratory Report No. 769-82. E.l. duPont de Nemours and Company, Inc. Haskell Laboratory for Toxicology and Industrial Medicine, Newark, DE.
133. Chemical Health Effects Assessment Methodology and Method to Derive Allowable Ambient Levels (1985) Massachusetts Department of Environmental Quality and Engineering. Draft.